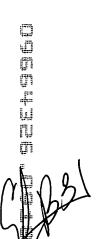
## We claim:

- 1. A hirudin precursor, comprising a signal sequence selected from signal sequences of an outer membrane protein of Serratia marcescens, an oprF protein of Pseudomonas fluorescens, a lamB protein of Escherichia coli, and a fumarate reductase of Shewanella putrifaciens, wherein aa<sub>x</sub>-hirudin is attached at the C-terminal of said signal sequence, wherein aa<sub>x</sub> represents an amino acid.
- 2. The precursor of claim 1, where said signal sequence is selected from a signal sequence of an outer membrane protein of *Serratia marcescens*, and a fumarate reductase of *Shewanella putrifaciens*.
- 3. The precursor of claim 1, wherein  $aa_x$  is leucine.
- 4. A process for preparing  $aa_x$ -hirudin, wherein  $aa_x$  is an amino acid, comprising:
- (a) preparing a hirudin precursor comprising a signal sequence selected from signal sequences of an outer membrane protein of Serratia marcescens, an oprF protein of Pseudomonas fluorescens, a lamB protein of Escherichia coli, and a fumarate reductase of Shewanella putrifaciens, wherein aa<sub>x</sub>-hirudin is attached at the C-terminal of said signal sequence,
- (b) preparing an expression plasmid comprising a DNA sequence coding for said hirudin precursor;
- (c) expressing said expression plasmid from (b) in a suitable *E. coli*, wherein said *E. coli* is in a culture medium;
- (d) secreting said selected hirudin precursor from said *E. coli*, wherein said selected hirudin precursor is simultaneously processed; and
- (e) isolating  $aa_x$ -hirudin from the culture medium.
- 5. The process of claim 1, wherein  $aa_x$  is leucine.



- 6. A process for selecting a suitable signal pertide for secretory expression of a desired protein in *E. coli*, comprising:
- (a) expressing in *E. coli* in culture medium, hirudin or a hirudin derivative which has antithrombotic activity, and which has a defined amino acid, aa<sub>x</sub>, at its N terminus, wherein said amino acid aa<sub>x</sub> is connected via its N-terminal to a signal peptide to be tested;
- (b) determining expression rate by measuring said protein activity in the culture supernatant;
- (c) repeating steps (a) and (b) with various signal peptides;
- (d) selecting said suitable signal peptide by comparing the expression rates represented by the hirudin antithrombotic activity found in step (b).
- 7. The process of claim 6, wherein  $aa_x$  is leucine.
- 8. The process of claim 6, further comprising expressing said suitable signal peptide and the desired protein in *E. coli* via a nucleic acid construct, wherein expression of the desired protein and said suitable signal peptide occurs with simultaneous elimination of said suitable signal peptide.
- 9. The process of any one of change of the state of the desired protein is hiruding
- 10. A process of efficiently producing a desired protein comprising:
- (a) selecting a suitable signal peptide according to the process of claim 6;
- (b) preparing a nucleic acid construct coding for a precursor protein consisting of the suitable signal peptide from step (a) and the desired protein; and
- (c) expressing the nucleic acid construct of step (b) in *E. coli*, wherein the selected suitable signal peptide is simultaneously eliminated.

- 11. The process of claim 10, further comprising isolating the desired protein from culture supernatant.
- 12. The process of claim 10 wherein  $aa_x$  is leucine.
- 13. The process of claim 10, wherein said nucleic acid construct has a sequence coding for said selected signal peptide selected from an outer membrane protein of Serratia marcescens, an oprF protein of Pseudomonas fluorescens, a lamB protein of Escherichia coli, and a fumarate reductase of Shewanella putrifaciens.
- 14. The process of any one of claims 10, 11, 12, or 13, wherein the desired protein is hirudin.